Remarks

In view of the foregoing amendments, reconsideration and withdrawal of the outstanding Office Action rejections is respectfully requested. Claim 19 has been amended and claim 36 has been added. No new matter is added.

Response to Rejections under 35 U.S.C. § 112

Claims 10, 12, 14, 17-19, and 35 were rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. The Examiner asserts that Voskoglou-Nomikos does not teach that studies of cell lines are predictive for methods of reducing invasivity of cancer cells and indicates that panels of cell lines are required to provide predictive information and that the data may not be applicable to non-cytotoxic drugs (see paragraph bridging pages 4235-4236). Further, the Examiner asserts that although Khleif teaches that animal models are generally acceptable in drug development, no evidence has been presented that demonstrates that an antibody or other agent against AXL can reduce the invasivity of cancer cells *in vivo*. The Examiner contends that the presented *in vivo* data does not show a purely *in vivo* effect because tumor cells were altered *in vitro* (truncation of UFO/AXL) prior to implantation.

Submitted herewith is a declaration signed by Dr. Thore Hettmann presenting experimental data which shows the effects of rat anti-AXL antibodies on human prostate carcinoma growth in nude mice. Specifically, PC-3-LN prostate carcinoma cells were implanted into the prostate of $NMRI^{-nu/nu}$ mice. Compared with a control antibody, the rat anti-AXL antibody reduced overall growth of PC-3-LN prostate tumors in nude mice (see Figure 1 of the declaration).

Further, the data presented herewith shows that the anti-AXL antibody reduced the occurrences of spleen metastases compared with control, as well as the known cancer drug Sutent® (see Figure 2 of the declaration).

Thus, Dr. Hettmann concludes that the presented data has demonstrated effective reduction in the invasiveness of non-altered tumor cells implanted in mice by administering an AXL inhibitor *in vivo*.

Applicants submit that the above data demonstrations the effective reduction of invasivity of unaltered tumor cells implanted in an animal by administering an AXL inhibitor or antibody as requested by the Examiner. Therefore, Applicants believe that claims 10, 12, 14, 17-19, and 35 do provide enabling disclosure. Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

Claim 19 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner asserts that it is not clear what the limitation "the inhibitor" in claim 19 refers to because claim 10, upon which claim 19 depends, is drawn to "an inhibitor of the AXL gene, AXL ligand gene, AXL protein, and/or AXL protein ligand". Applicants submit that claim 19 has been amended to recite "...wherein at least one of the AXL protein inhibitor and the AXL protein ligand inhibitor is an antibody directed against the AXL protein". Thus, Applicants submit that claim 19 is now definite and clear and respectfully request that the rejection be withdrawn.

Claims 10, 12, 14, 17, 18, and 35 have been rejected under 35 U.S.C. 112, second paragraph, as failing to comply with the written description requirement. The Examiner asserts that the specification does not define any structural features commonly possessed by members of the genus "inhibitor of the AXL protein". Applicants submit that there is written support for inhibitors of the AXL protein on page 6, line 16 to page 8, line 4 of the specification. Those skilled in the art at the time of filing would know how to produce antibodies, proteolytic fragments, e.g. Fab, Fab', or Fab2 fragments, scFV fragments, biologically active nucleic acids, peptides, low molecular weight AXL kinase inhibitors, AXL analogues, etc. based on the DNA sequence of the AXL gene and the protein sequence of AXL which were publicly available at the time of filing. Therefore, Applicants submit that the specification as filed provides satisfies the written description requirement for a method of reducing the invasivity of cancer cells in a subject in need thereof. Therefore, Applicants respectfully request that the rejection of claims 10, 12, 14, 17, 18, and 35 be withdrawn.

New Claims

New claim 36 has been added to define a further embodiment of the invention. Support for this claim can be found in the paragraph bridging pages 6 and 7.

Conclusions

In view of the above amendments and remarks hereto, Applicants believe that all of the Examiner's rejections set forth in the January 26, 2009 Office Action have been

fully overcome and that the present claims fully satisfy the patent statutes. Applicants, therefore, believe that the application is in condition for allowance. The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

By 

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RBM/AH
Enclosure: Declaration of Dr. Hettmann
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